

Development and validation of UV- Spectrophotometric methods for simultaneous estimation of Paracetamol and Ibuprofen in bulk and tablet dosage form

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Abstract: Two simple, rapid, accurate, precise, and economic spectrophotometric methods for simultaneous estimation of Paracetamol and Ibuprofen in pure and tablet dosage form have been developed. Method I is based on the simultaneous equation method. Paracetamol and Ibuprofen show absorbance maximums at 256 and 222.4 nm respectively, so absorbance was measured at the same wave lengths for the estimation of Paracetamol and Ibuprofen. Method II is based on determination of Q-value. Absorbance is measured at 226.4 nm (Isoabsorptive point) and 222.4nm (λ_{max} of Ibuprofen). Both drugs obey the Beer Lambert's law in the concentration range of 5-30 $\mu\text{g/mL}$. Methods are validated according to ICH guidelines.

Keywords: Paracetamol, Ibuprofen, Simultaneous equation, Absorbance ratio, Validation.

INTRODUCTION:

Paracetamol is a commonly used medicine that can help treat pain and reduce a high temperature (fever). It's typically used to relieve mild or moderate pain, such as headaches, toothache or sprains, and reduce fevers caused by illnesses such as colds and flu. Paracetamol is often recommended as one of the first treatments for pain, as it's safe for most people to take and side effects are rare. Paracetamol works as a painkiller by affecting chemicals in the body called prostaglandins. Prostaglandins are substances released in response to illness or injury. Paracetamol blocks the production of prostaglandins, making the body less aware of the pain or injury. Paracetamol reduces temperature by acting on the area of the brain that is responsible for controlling temperature. Babies and children can be given paracetamol to treat fever or pain if they are over two months old. **Ibuprofen** is a painkiller, which is available over-the-counter, without a prescription. It is one of a group of painkillers called non-steroidal anti-inflammatory drugs (NSAIDs), and can be used to: ease mild to moderate pain – such as toothache, migraines and period pain. **Ibuprofen** is used in a very similar way to **Paracetamol**; it treats pain but can also be used to treat fever. The main difference is that **Ibuprofen** reduces inflammation. **Ibuprofen** is a type of drug called a non-steroidal anti inflammatory (NSAID). This means that **Ibuprofen** will reduce inflammation. The review of literature revealed that the combined dosage form has been estimated by spectrophotometric method by using methanol as solvent. This paper describes two simple, rapid, accurate, precise and economical methods for simultaneous determination of paracetamol and ibuprofen in tablet dosage form.

MATERIALS AND METHODS:

Instruments

Double beam UV-visible spectrophotometer model Jasco V-530 using spectra manger software. The spectra were recorded over range 200-400nm against solvent in 1 cm quartz cells.

Materials

Pure paracetamol was kindly gifted from Zest pharma, Indore and ibuprofen from Wanbury ltd. Navi Mumbai. The commercially available tablets, Combiflam (Label claim: paracetamol- 325 mg, ibuprofen- 400 mg) was procured from local market. All the chemicals and reagents were of analytical grade.

Selection of common solvent

After checking the solubility of drugs in different solvents. Methanol has been selected as common solvent for developing this methods.

Selection of wavelength.

The overlain spectrum of Ibuprofen and Paracetamol in 0.1N NaOH is shown in Fig 1. The dilution was obtained to the concentration of 10 $\mu\text{g/ml}$ for both paracetamol and ibuprofen solution. The study of spectrum of paracetamol show a λ_{max} at 256

nm whereas ibuprofen shows at 222.4 nm. These two wavelengths were selected for development of simultaneous equation. From the overlain spectrum, it is evident that isoabsorptive point is at 226.4 nm for absorbance ratio method.

Preparation of standard stock solution

Accurately weighed 10 mg of Paracetamol and Ibuprofen were transferred into volumetric flasks separately and then volume was made up to 10 ml with methanol to get a concentration of 1000 µg/ml for all two drugs. Standard stock solution (1000 µg/ml) was further diluted with methanol to obtain 5-30 µg/ml for Paracetamol and Ibuprofen

Method I (Simultaneous equation method)

Two wavelengths selected for the development of the simultaneous equations are 256 nm and 222.4 nm. The absorptivity values determined for paracetamol are 0.0531 (ax1), 0.0123 (ax2) and for ibuprofen are 0.0065 (ay1), 0.0441 (ay2) at 256 nm and 222.4 nm respectively. These values are means of six estimations. The absorbances and absorptivity at these wavelengths were substituted in equation 1 and 2 to obtain the concentration of both drugs.

$$C_X = A_2 \times 0.0065 - A_1 \times 0.0441 / -0.00202 \text{ ----- equ. 1}$$

$$C_Y = A_1 \times 0.0531 - A_2 \times 0.0123 / -0.00202 \text{ ----- equ. 2}$$

Method II (Absorbance ratio method)

From the overlain spectrum of Paracetamol and Ibuprofen, two wavelengths were selected the isoabsorptive point is 226.4 nm. The method employed Q -values, and the concentrations of drugs in sample solutions were determined using the following equations:

$$C_1 = \frac{Q_{\square} - Q_y}{Q_x - Q_y} \times \frac{A_1}{ax_1} \text{equation 1.}$$

$$C_2 = \frac{Q_{\square} - Q_x}{Q_y - Q_x} \times \frac{A_2}{ay_1} \text{equation 2.}$$

Where, A_1 and A_2 are the absorbances of mixture at 256 and 222.4 nm, $Q_{\square} = A_2 / A_1$, $Q_y = ay_2 / ay_1$ and $Q_x = ax_2 / ax_1$, ax_1 (0.1432), ax_2 (1.1432), ay_1 (0.8173) and ay_2 (2.4322) are absorptivities (1%, 1 cm) of Paracetamol and Ibuprofen.

Analysis of the tablet formulations

Twenty tablets of marketed formulation were accurately weighed and powdered. A quantity of powder equivalent to 50 mg of paracetamol was transferred to 100 mL volumetric flask and dissolved in Methanol and final volume was made up with Methanol. The sample solution was then filtered through Whatman filter paper No.41. From the above solution 10 mL of solution was taken and diluted to 50 mL with Methanol to get a solution containing 100 µg/mL of paracetamol and corresponding concentration of ibuprofen. From above, 0.65 mL of solution was diluted with same solvent in 10 mL volumetric flask to get final concentration of paracetamol 6.5µg/mL and ibuprofen 8µg/mL. Analysis procedure was repeated six times with tablet formulation. The results of tablet analysis are reported in Table 2.

Validation of the developed methods:

For each drug, appropriate dilutions of standard stock solutions were assayed as per the developed methods. For method I and II, the Beer- Lambert's concentration range was found to be 5-30 µg/mL for both drugs. The linearity data for both methods are presented in Table 1.

Accuracy

To check the accuracy of the proposed method, recovery studies were carried out 50, 100 and 150% of the test concentration as per ICH guidelines. The recovery study was performed three times at each level. The result of the recovery studies are reported in table 3.

Precision:

Repeatability

To check the degree of repeatability of the methods, suitable statistical evaluation was carried out. Repeatability was performed for six times with tablets formulation. The standard deviation, coefficient of variation and standard error was calculated. The results of statistical evaluation are given in Table 2.

Intermediate Precision (Interday and Intraday precision)

The interday and intraday precision was determined by assay of the sample solution on the same day and on different days at different time intervals respectively. The results of the same are presented in Table 4.

RESULT AND DISCUSSION:

Linearity range for paracetamol and ibuprofen are 5-30 µg/mL at respective selected wavelengths. The coefficient of correlation for paracetamol at 256 nm and for ibuprofen at 222.4 nm is 1 and 0.999 respectively. Both drugs show good regression values at their respective wavelengths and the results of recovery study.

Table No. 1: Optical parameters and regression characteristic

Parameters	Parameters Paracetamol at λ_{max}	Ibuprofen at λ_{max}	Paracetamol at iso-absorptive point	Paracetamol at iso-absorptive point
Beer's Law range	5-30 $\mu\text{g/mL}$	5-30 $\mu\text{g/mL}$	5-30 $\mu\text{g/mL}$	5-30 $\mu\text{g/mL}$
Regression Equation (Y)	$Y = 0.053x + 0.011$	$Y = 0.054x + 0.012$	$Y = 0.023x + 0.011$	$Y = 0.034x + 0.011$
Slope (m)	0.044	0.423	0.0012	0.311
Intercept (c)	0.002	0.113	0.021	0.012
Correlation coefficient	0.988	0.999	0.999	0.988

Table No. 2: Analysis of Tablet Formulation

Sr. No.	Drug Name	Labelled Amount (mg)	S.D.	%COV
1	Paracetamol	400	0.5602	100%
2	Ibuprofen	325	0.0025	98.55%

Table No. 3: Result of recovery study

Sr. No.	Drug	Concentration of standard added	S.D.	%RSD	%Recovery
1	Paracetamol	50%	0.0077	1.63	100.07%
		100%	0.0429	1.74	102.65%
		150%	0.0158	0.40	99.07%
2	Ibuprofen	50%	0.0028	0.29	98.40%
		100%	0.0037	0.68	100.83%
		150%	0.0047	1.20	1.91%

Sr. No.	Drug	Concentration of standard added	S.D.	%RSD	%Recovery
1	Metformin HCL	80%	0.0067	1.73	100.07%
		100%	0.0359	1.84	104.65%
		120%	0.0068	0.30	99.07%
2	Voglibose	80%	0.0018	0.19	97.40%
		100%	0.0067	0.78	100.83%
		120%	0.0087	1.10	100.91%

Table No. 4: Validation parameters

Sr. no	Parameter	S.D.		% RSD	
		PARA	IBU	PARA	IBU
1.	Drug	PARA	IBU	PARA	IBU
2.	Repeatability	0.0057	0.0021	0.28	0.38
3.	Interday Precision	0.0096	0.7578	0.58	0.47

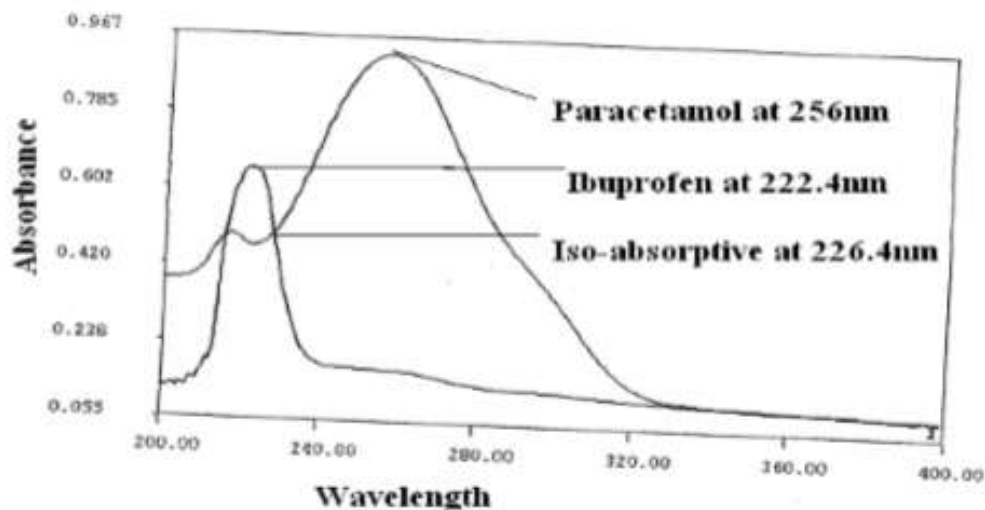


Fig.1 overlain spectra of paracetamol and ibuprofen

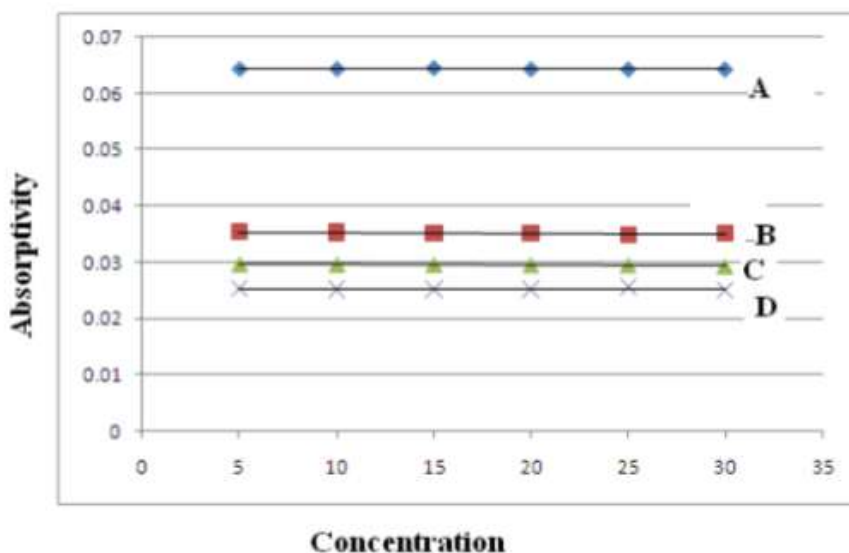


Fig.3 Response ratio curve A-Paracetamol at 256nm, B-Ibuprofen at 222.4nm, C-Paracetamol-226.4nm and D-Ibuprofen at 226.4nm

Fig.2. Response ratio curve A-Paracetamol at 256nm, B-Ibuprofen at 222.4nm, C-Paracetamol-226.4nm and D-Ibuprofen at 226.4nm.

CONCLUSION:

In this work, a new UV-Spectrophotometric method has developed and validated for Paracetamol & Ibuprofen by Absorbance ratio method and simultaneous equation method. The results of present study indicate that the proposed UV-Spectrophotometric method is simple, rapid, precise and accurate. The developed UV-Spectrophotometric method was found suitable for determination of Paracetamol & Ibuprofen in tablet dosage form. They can be easily applied in quality control laboratory tests in the dosage form.

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